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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,053	10/19/2001	Apollon Papadimitriou	CIBT-P01-097	4732
28120	7590	09/09/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			O HARA, EILEEN B	
			ART UNIT	PAPER NUMBER
			1646	
DATE MAILED: 09/09/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

MS

## Office Action Summary

### Application No.

09/890,053

### Applicant(s)

PAPADIMITRIOU ET AL.

### Examiner

Eileen O'Hara

### Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-4,7-9 and 11-15 is/are pending in the application.
- 4a) Of the above claim(s) 9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,7,8 and 11-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-4,7-9 and 11-15 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- 1) ☐ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Claims 1-4, 7-9 and 11-15 are pending in the instant application. Claims 1, 7 and 8 have been amended, claims 5, 6 and 10 have been canceled and claims 11-15 have been added as requested by Applicant in the Paper filed June 1, 2004.

Claim 9 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-4, 7, 8 and 11-15 are currently under examination.

### ***Claim Objections***

2. Claims 7 and 11-15 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Because claim 7 was previously examined, it will be examined in this office action. However, new claims 11-15 have not been further treated on the merits.

### ***Double Patenting***

3. Claims 1-4, 7 and 8 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,207,718, for reasons of record in the Office Action, Paper No. 10, at pages 5-6.

Applicant's traverse the rejection on page 4 of the response and assert that the amendments to the claims more particularly point out certain embodiments of the invention, and that the amendments are believed to obviate the need for a terminal disclaimer. Applicants' arguments have been fully considered but are not deemed

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persuasive. The scope of the patented and instant claims differs in the combinations of carriers and additives recited, however the patented claims recite carriers and additives that are also recited in the instant claims. For example, claim 1 recites a specific range of hedgehog concentrations and pH range, while the hedgehog concentration and pH range are recited in different claims in the patent. It would clearly be obvious to combine the two in one claim, and it would clearly be obvious to combine the other recited elements. For these reasons, the rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-4, 7 and 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Pepinsky et al., U.S. Patent No. 6,444,793, filed 12/3/97, (provisionals filed 9/10/98,

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6/17/98, 3/20/98 and 12/3/97) in view of Easton et al., U.S. Patent No. 4,614,794, issued Sept. 30, 1986, and further in view of Usala et al., U.S. Patent No. 6,231,881, filing date July 10, 1998, for reasons of record in the previous Office Actions, Paper No. 10 at pages 7-11, paper mailed Jan. 29, 2004 at pages 3-5, and below.

Applicants traverse the rejection on pages 5-6 of the response, and assert that the combination of references cited by the Examiner fails to render the claimed invention obvious, and although broadly enabling, the teachings of Pepinsky et al. fail to disclose the particular combinations of elements that characterize the claimed invention, and that Easton et al. or Usala et al. do not overcome the deficiencies of Pepinsky et al., and merely provide nothing more than an invitation to one of skill in the art to attempt to arrive at Applicants' invention. Applicants argue that there is no motivation to specifically select the particular concentrations of hedgehog proteins, the particular buffers, the particular pH range, or the particular delayed release characteristics claimed.

Applicants' arguments have been fully considered but are not deemed persuasive.

Pepinsky et al. provides ample motivation for one of skill in the art to determine concentrations of hedgehog proteins, particular buffers, particular pH ranges and delayed release biodegradable proteins. Pepinsky et al. teaches that the half-life of hedgehog is very short after systemic application and that multiple injections are required to achieve a robust response to the protein and that the possibility of formulation in liposomes provides a means of achieving a response with fewer treatments (column 38, line 62 to column 39, line 1), and that the proteins can be administered locally to the site of bone fractures to help heal those fractures (column 39, lines 20-22). Since Easton teaches complexes having different stabilities, pore sizes and uses (column 3, line 47 to column

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4, line 28), and that examples of such applications include media to be used in the controlled release of physiologically active compounds (column 5, lines 50-55), it would have been *prima facie* obvious to one of ordinary skill in the art to administer the hedgehog proteins of Pepinsky et al. in a carrier such as collagen that has been formulated to release the proteins slowly as taught by Easton. The motivation to do so is provided by Pepinsky's teachings that systemically administered hedgehog proteins have short half-lives and that local application without the need for frequent application would be desirable under certain circumstances. Although Pepinsky et al. do not specifically state that the specific compositions of the instant claims, Pepinsky et al. provide ample guidance on how to determine optimal pharmaceutical compositions, and that one of ordinary skill in the art would know how to make such determinations.

Applicants cite Corning Glass Works v. Sumitomo Electric U.S.A. on page 5 of the response, and assert that a valid patent may issue for a nonobvious species related to a prior patented invention, even though the improvement falls within the claims of that prior patent. From reading the case, the Examiner assumes that Applicants intend that the optical waveguide fiber (species) of Corning Glass Works patent 3,659,915 was found to be a nonobvious species of United Kingdom Patent No. 1,113,101, which disclosed optical fibers (genus). Applicants' statement on page 5 that a prior genus which does not explicitly disclose a species does not anticipate a later claim to that species is not disputed. However, that situation is not analogous to the present case. For example, a hedgehog concentration range of 0.1-100 mg/ml is a 1000 fold range, and cannot be considered a "species", and a pH buffered range of 6-8 is not unusual or unexpected since pH 6-8 would be considered physiological. Additionally, in the instant situation, the

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asserted “species” are clearly obvious over the prior art, as discussed above. Therefore, the rejection is maintained.

It is believed that all pertinent arguments have been answered.

### ***Conclusion***

5. No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (571) 272-

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0878. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.ispto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Eileen B. O'Hara, Ph.D.

Patent Examiner

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